REMARKS

Claims 39 and 42 have been amended to replace the code name CCI-779 with the chemical name temsirolimus. The common chemical name of temsirolimus for the code name CCI-779 and its structure are well-known to those of skill in the art. As such, no new matter has been introduced. Claim 41 has also been amended.

Claims 30-34, 37-39, 41-48, 50-56, 63-75, 122-125, 127-130, 132, and 134 are pending. Claims 75, 122-125, 127-130, 132, and 134 stand withdrawn.

Applicants have carefully considered all rejections but respectfully submit that the claims are allowable for the following reasons.

Withdrawn Claims

The Examiner has again failed to address Applicants' traversal of the withdrawal from consideration of Claims 75, 122-125, 127-130, 132 and 134 for allegedly being directed to non-elected subject matter. Applicants once again respectfully reiterate their traversal and request that the Examiner address this issue.

With respect to withdrawn Claim 75, Applicants had elected "rapamycin and analogs and derivatives thereof" and "wet form of age-related macular degeneration" in response to the Examiner's species election requirement. As stated in their election, then pending Claims 30-75 encompassed these species. In the July 6, 2007 Office Action, the Examiner examined Claim 75, which depends from Claim 68. Thus, the Examiner has already recognized that Claim 75 is directed to the elected subject matter and Applicants respectfully request that Claim 75 be restored to non-withdrawn status.

With respect to Claims 122-125, 127-130, 132, and 134, these claims depend from examined Claims 30, 38, 39, 43, 51, 57, or 63 and are directed to and read on the elected species. Accordingly, Applicants respectfully request that Claims 122-125, 127-130, 132, and 134 also be examined.

Rejections under § 112 – Indefiniteness

The Examiner rejected Claims 39, 41-48, and 50-56 under 35 U.S.C. § 112, ¶ 2 as being indefinite. The Examiner argued that the terms "CCI-779", "AP23841", and "ABT-578" are indefinite because they do not recite chemical structures or a name of the compounds. Claims 39 and 42 have amended to remove "ABT-578" and "AP23841" and to recite the commonly-known

chemical name for "CCI-779." As such, Applicants respectfully submit that Claims 39 and 42 and the claims that depend from them are definite.

Rejections under § 103

The Examiner rejected Claims 30-34, 37-39, 41-48, 50-56, and 63-74 under 35 U.S.C. § 103(a) as being obvious over Mollison (US 6,015,815) in view of Kulkarni (US 5,387,589) and Hu et al. (US 5,800,807). The Examiner argued that Hu et al. teaches the use of propylene glycol as a safe delivery vehicle for ophthalmic drugs.

Claims 30 and 38 recite a composition comprising rapamycin and polyethylene glycol suitable for ophthalmic administration by injection. Claim 39 recites a composition comprising rapamycin, tacrolimus, everolimus, pimecrolimus, CCI-779, or AP23841 in combination with polyethylene glycol suitable for ophthalmic administration by injection. Claims 51 and 63 recite methods of treatment comprising administering a composition comprising rapamycin and polyethylene glycol into the vitreous or between the conjunctiva and the sclera of an eye. None of the cited art, alone or in combination, teach or suggest all of these recited features.

As a first matter, Applicants note that none of the claims recite propylene glycol. Thus, the Examiner's assertion that Hu et al. discloses ophthalmic use of propylene glycol is irrelevant. Even if the Examiner intended to refer to polyethylene glycol instead of propylene glycol, Hu et al. still fails to teach the limitations that are missing from Mollison and Kulkarni. Specifically, Hu et al. only teaches use as a demulcent (i.e, an agent that forms a film over the outer membrane of the eye). Thus, Hu et al. only teaches topical administration to the eye. In contrast, Claims 30, 38, and 39 recite a composition that is suitable for administration by injection and Claims 51 and 63 recite administration into the vitreous or between the conjunctiva and the sclera of an eye. There would be no reason for one of skill in the art to take the teachings of Hu et al. regarding compositions for topical eye administration and modify them for administration into the interior of the eye. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) ("it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.")

Filed herewith is a Declaration of Dr. David Weber pursuant to 37 C.F.R. § 1.132. Dr. Weber states that those of skill in the ophthalmic arts would not have used a hygroscopic agent such as polyethylene glycol for administration into an eye. Specifically, if such a composition

was administered into the vitreous, it would have been expected to pull water into the eye ball leading to a deleterious increase in intraocular pressure and desiccation of retinal tissues. If the composition was administered by subconjunctival injection, it would have been expected to pull water out of the eye ball, leading to a deleterious decrease in intraocular pressure and swelling. Thus, as Dr. Weber states, one of skill in the art would not have used polyethylene glycol for administration into the eye over concerns of disruption of vision or damage to the eye. Furthermore, Dr. Weber points out that all compositions that are currently administered into the eye are aqueous based. Finally, Dr. Weber notes that one of skill in the art would have been disinclined to use polyethylene glycol for ophthalmic injection because it would have been expected to require a large gauge needle creating a hole into the eye.

Based on Dr. Weber's declaration, one of skill in the art would have considered a polyethylene glycol composition ***unsuitable*** for administration into the eye. The teachings of Hu et al. regarding topical eye administration would not have altered this view. Specifically, topical administration of a hygroscopic agent to the outer membranes of the eye would not be expected to cause the deleterious effects discussed in the Dr. Weber's declaration. Thus, Hu et al. does not contradict the view held by those of skill in the art that polyethylene glycol would have been unsuitable for administration into the eye. As such, Applicants respectfully submit that Claims 30, 38, 39, 51, and 63 and the claims that depend from them (i.e., Claims 30-34, 37-39, 41-48, 50-56, and 63-74) are not obvious over the cited art. The cited art fails to teach or suggest all limitations of the claims and there would be no reason to modify the teachings to arrive at the recited claims.

In addition, Claim 51 recites a method of treating the wet form of age-related macular degeneration by administering rapamycin into the eye. Similarly, Claim 63 recites a method of inhibiting the transition of the dry form of age-related macular degeneration to the wet form by administering rapamycin into the eye. As Applicants noted in their previous responses, Mollison teaches to use tetrazole-containing compounds that are chemically distinct from rapamycin. Mollison teaches that these compounds can be used to treat not less than about 175 distinct diseases or conditions, including diseases as diverse as gastric ulcers and gingivitis. *See* column 8, line 51 to column 10, line 64. No one of skill in the art would actually believe that the tetrazole-containing compounds of Mollison could be used to treat all of these diseases or

conditions. Nonetheless, even taking this disclosure at face value, it does not teach that rapamycin would be useful for all these indications. When rapamycin is discussed in the background section of Mollison, the only diseases it is associated with are fungal infections, tumors, multiple sclerosis, rheumatoid arthritis, and organ graft rejection.

Notably, several of the significant side effects caused by rapamycin are conditions that Mollison teaches are treated by the tetrazole-containing compounds. For example, it was known that administration of rapamycin can ***cause*** acne and thrombocytopenia. *See e.g.,* Rapamune package insert pages 12-14 and Vasquez, E., "Sirolimus: A new agent for the prevention of renal allograft rejection," *Am. J. Healty-Syst. Pharm.*, vol. 57, pages 443-444 (2000) (Exhibit A). However, Mollison teaches that its tetrazole-containing compounds can be used to ***treat*** acne and thrombocytopenia. Mollison, column 9, lines 7 and 36. Thus, one of skill in the art would know that rapamycin ***cannot*** be used to treat all of the indications listed in Mollison. As such, the skilled artisan would have no reason to believe that rapamycin could be used to treat the wet form of age-related macular degeneration or inhibit the transition of the dry form of age-related macular degeneration to the wet form based on the teachings of Mollison.

Given the differences between the asserted uses of the tetrazole-containing compounds of Mollison and the known uses (and side effects) of rapamycin, one of skill in the art would not have chosen rapamycin for the investigation of other compounds useful to treat the same indications. Instead, since rapamycin was known to not be effective for (and indeed be adverse to) the treatment of some of the indications listed in Mollison as well as the fact that Mollison teaches away from using rapamycin (see column 8, lines 35-38), one of skill in the art would have chosen a different analog when looking for alternative compounds. As pointed out by the Federal Circuit in *Eisai Co. Ltd. V. Dr. Reddy's Labs Ltd.*, 533 F.3d 1353 (Fed. Cir. 2008), obviousness based on a chemical analog requires that there be "some reason that would have led a chemist to modify a known compound in a particular manner" to achieve "identified, predictable solutions." Since it was known that rapamycin could not be used as a "solution" to treat all of the indications listed in Mollison, there would have been no reason to choose rapamycin as an alternative.

Finally, Applicants reiterate that none of the cited art teach inhibiting the transition of the dry form of age-related macular degeneration to the wet form as recited in Claims 63-67. The

Examiner appears to respond to this argument by noting Applicants' alleged election of macular degeneration. While the relevance of Applicants' species election is not apparent, Applicants note that their election was in fact the "wet form of age-related macular degeneration."

Based on all of the foregoing reasons, Applicants respectfully submit that Claims 30-34, 37-39, 41-48, 50-56, and 63-74 are not obvious over the cited art.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

By the foregoing amendments and remarks, the Applicants respectfully submit that they have overcome the Examiner's rejections and request a timely issuance of a Notice of Allowance. If there are any remaining issues that can be resolved via telephone conversation, the Examiner is invited to call the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: May 17, 2010

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